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EXAMINER	
SKELDING, ZACHARY S	
ART UNIT	**PAPER NUMBER**
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/526,072	SUGIMURA ET AL.	
	Examiner	Art Unit	
	Zachary Skelding	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *1,2,12-19 and 23-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-11 and 20-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 2/28/05 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5-27-05 3-24-06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election of Group II and applicant's election of species, with traverse, is acknowledged.

   Claims 1-33 are pending.

2. Applicant's provision of Sequence Listing, and computer readable form filed September 1, 2005 is acknowledged.

3. Applicant's election with traverse of Group II, drawn to gene fragments encoding anti-IL-6 antibodies and the species of scFv gene fragment wherein the scFv gene fragment does not comprise a portion of the human antibody CH/CL chain in the reply filed July 27, 2007 is acknowledged.

   The traversal of the Groups of inventions is on the ground(s) that according to applicant even if the broadest subject matter presently claimed by applicants were unpatentable over Ito this still would not destroy unity of invention, because there is unity between the two groups in the basis of the same or corresponding technical features more narrowly claimed.

   This is not found persuasive because the claims as originally presented were the claims that the examiner evaluated for unity of invention, not some subset of claims "more narrowly claimed", and the claims as presented lacked unity of invention for the reasons record.

   The traversal of the species election is on the grounds that they are "...entitled to have their generic claims examined and considered as a whole. Applicants do not deny that the species may be patentably distinct from one another. However, applicants submit and maintain that the PTO has no authority for requiring an applicant to break apart a generic claim into individual claims, as that would in effect amount to a rejection. If applicants generic claims meet the requirements for patentability, including those of §§102, 103 and 112, then the generic claims should be allowed."

   This is not found persuasive because applicant agrees "the species may be patentably distinct from one another," and because applicant's argument about breaking apart a generic claim are not found convincing. It is not clear from applicant's argument what, if any, generic claim is being denied examination by this election of species requirement.

   Moreover, contrary to applicant's argument, should the elected species be found allowable applicant will be entitled to examination of the non-elected species as set forth in MPEP § 821.04: The propriety of a restriction requirement should be reconsidered when all the claims directed to the elected invention are in condition for allowance, and the nonelected invention(s) should be considered for rejoinder. Rejoinder involves withdrawal of a restriction requirement between an allowable elected invention and a nonelected invention and examination of the formerly nonelected invention on the merits.

Therefore one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of "a gene fragment...binds to human IL-6 and inhibits the biological activities thereof," or the nature or parameters by which to determine said metes and bounds.

Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 3-11 and 20-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a gene fragment coding for a single chain Fv that binds human IL-6 wherein said gene fragment consists of a gene fragment coding for a Vh chain bound to gene fragment coding for a Vl chain, or a gene fragment coding for a single chain Fv that binds human IL-6 wherein said gene fragment consists of a gene fragment coding for a Vh chain bound to gene fragment coding for a Vl chain, wherein CDR1 to CDR3 of Vh are SEQ ID NOs: 5-7 and/or CDR1 to CDR3 of Vl are SEQ ID NOs: 8-10 or a gene fragment coding for a single chain Fv that binds human IL-6 wherein said gene fragment consists of a gene fragment coding for a Vh chain bound to gene fragment coding for a Vl chain, wherein said Vh chain is SEQ ID NO: 2 and said Vl chain is SEQ ID NO: 4, and wherein the above mentioned gene fragments inhibit the IL-6 dependent proliferation response of IL-6 dependent cell line KT-3 **does not reasonably provide enablement for** gene fragments coding for a VH chain or a VL chain of a human anti-human IL-6 antibody, wherein said gene fragments comprise, for example, anything from a single CDR from a Vh or Vl to a full length Vh or Vl, or gene fragments coding for a single chain Fv human anti-human IL-6 antibody consisting of defined Vh and Vl genes wherein the gene fragments comprise amino acid deletions and/or substitutions and/or additions in the Vh and/or Vl chains, without an upper limit on the number of changes, and wherein the above mentioned gene fragments inhibit any or all IL-6 biological activities. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The disclosure of the specification does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in In re Wands, 8 USPQ2d 1400 (CA FC 1988). Wands states on page 1404, "Factors to be considered in determining whether a disclosure would require undue experimentation have

been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The instant claims, given their broadest reasonable interpretation consistent with the instant specification, read on gene fragments "coding for a VH chain or a VL chain" of a human anti-human IL-6 antibody, wherein said gene fragments comprise, for example, anything from a single CDR from a Vh or Vl, to a full length Vh or Vl, to full length Vh or Vl and further encoding the complimentary Vh and Vl chains (see, for example, claims 3, and 9). The instant claims also read on various gene fragments, including those gene fragments consisting of defined Vh and Vl genes wherein said gene fragments comprise amino acid deletions and/or substitutions and/or additions in the Vh and/or Vl chains, without an upper limit on the number of changes given that the claims recite "one or several" and the meaning of "several" is not defined in the instant specification and therefore will be treated as without limit for the purposes of examination. The instant claims also recite that the IL-6 antibodies "bind to IL-6 and inhibit the biological activity thereof," however the meaning of the phrase "inhibit the biological activity thereof" is not defined by the instant specification and it is unclear exactly what this encompasses for the reasons put forth in the Section 5 above.

The instant specification discloses the production and screening of a phage scFv library based on human Vh and Vl cDNAs against human IL-6, the isolation of the IL6gk3-2 clone, which was sequenced to yield SEQ ID NOs: 2 (Vh), 4 (Vl), 5-7 (Vh CDRs 1-3) and 8-10 (Vl CDRs 1-3) and shown to have the ability to inhibit the IL-6 dependent proliferation response of IL-6 dependent cell line KT-3 (see pages 6-9 and Figure 3). The instant specification also discloses other IL6gk3- and 4- clones which do not appear to have been characterized other than measuring their ability to bind IL-6 (see Figure 1).

However, the specification does not give sufficient direction or guidance for the skilled artisan to go about making a gene fragments coding for a VH chain or a VL chain of a human anti-human IL-6 antibody, wherein said gene fragments comprise, for example, anything from a single CDR from a Vh or Vl to a full length Vh or Vl, or gene fragments coding for a single chain Fv human anti-human IL-6 antibody consisting of defined Vh and Vl genes wherein the gene fragments comprise amino acid deletions and/or substitutions and/or additions in the Vh and/or Vl chains, without an upper limit on the number of changes.

In order to be eligible for rejoinder, a claim to a nonelected invention must depend from ***or otherwise require all the limitations of an allowable claim.*** A withdrawn claim that does not require all the limitations of an allowable claim will not be rejoined...In order to retain the right to rejoinder, applicant is advised that the claims to the nonelected invention(s) should be amended during prosecution to require the limitations of the elected invention. ***Failure to do so may result in a loss of the right to rejoinder.***

Rejoined claims must be fully examined for patentability in accordance with 37 CFR **1.104**. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. **101**, **102**, **103** and **112**.

The restriction requirement is still deemed proper and is therefore made FINAL.

Thus, claims 3-11 and 20-22 are under examination as they read on a gene fragment encoding an anti-IL-6 antibody, including an anti-IL-6 scFv antibody, wherein the elected species of anti-IL-6 scFv antibody is an scFv that does not comprise a portion of the human antibody CH/CL chain.

Moreover, claims (1, 2, 16-19, 29, 32 and 33) and further claims (12-15, 23-28, 30 and 31) are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention or a nonelected species of invention, respectively, there being no allowable generic or linking claim.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 3-11 and 20-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims are indefinite in the recitation of "a gene fragment...binds to human IL-6 and inhibits the biological activities thereof," because the metes and bounds of "inhibits the biological activities thereof" is unclear and ambiguous.

While the instant specification discloses in the paragraph bridging pages 1-2 that IL-6 has diverse biological activities including induction or inhibition of cellular proliferation, induction of cellular differentiation, the specification does not define what is meant by an IL-6 biological activity. Moreover, IL-6 has additional biological properties of relevance not mentioned in the instant specification such as its ability to bind α2-macroglobulin (see Section 7 below). Moreover, the specification does not provide a standard for ascertaining the nature or parameters of what IL-6 biological activities are encompassed by the instant claims.

For example, the instant specification does not give direction or guidance to the skilled artisan as to how they should go about making an anti-IL-6 antibody using only the a gene fragment coding for a Vh domain having SEQ ID NOs: 5-7, see for example, claim 4. Likewise, the instant specification does not give direction or guidance to the skilled artisan as to which amino acids can be deleted and/or substituted and/or added to the Vh and/or Vl chains of a single chain Fv anti-IL-6 antibody consisting of a gene fragment coding for the Vh chain of SEQ ID NO: 2 and/or the Vl chain of SEQ ID NO: 4, without an upper limit on the number of changes given.

Thus, the teachings of the instant specification are extremely narrow relative to the broad scope of the claims at issue.

The scope of the claims must bear a reasonable correlation with the scope of enablement. See In re Fisher, 427 F.2d 833,839, 166 USPQ 18, 24 (CCPA 1970).

With respect to claims drawn to gene fragments encoding anti-IL-6 antibodies wherein said gene fragments containing fewer than all 6 CDRs or comprise amino acid deletions and/or substitutions and/or additions in the Vh and/or Vl chains, without an upper limit on the number of changes, it is established in the art that, in general, all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites (See Janeway et al., Immunobiology, 5th Ed., Garland Science, pp. 94-105 (2001)).

To further illustrate this point, consider Vajdos et al. (J Mol Biol. 2002 Jul 5;320(2):415-28) which teaches that, "[t]he specificity and affinity of an antibody for its cognate antigen is determined by the sequence and structure of the variable fragment (Fv): a heterodimer consisting of the N-terminal domains of the heavy and light chains. Even within the Fv, *antigen binding is primarily mediated by the complementarity determining regions (CDRs), six hypervariable loops (three each in the heavy and light chains) which together present a large contiguous surface for potential antigen binding.* Aside from the CDRs, the Fv also contains more highly conserved framework segments which connect the CDRs and are mainly involved in supporting the CDR loop conformations, although in some cases, framework residues also contact antigen. As an important step to understanding how a particular antibody functions, it would be very useful to assess the contributions of each CDR side-chain to antigen binding, and in so doing, to produce a functional map of the antigen-binding site." (see, page 416, column bridging paragraph, emphasis added).

Vajdos goes on to teach that "[b]y analyzing panels of point mutants, a detailed map of the binding energetics can be obtained, but the process can be *very laborious* because *individual mutant proteins must be made and analyzed separately*. In particular, *a comprehensive analysis* of an antigen binding site would ideally *encompass all CDR residues*, and this would require the analysis of dozens or even hundreds of point mutants." (see page 416, right column, first paragraph, emphasis added). Vajdos solution to this dilemma was to make use of a recently developed shotgun scanning mutagenesis which "uses phage displayed libraries of protein mutants constructed using degenerate codons with restricted diversity." While this "recently developed shotgun scanning mutagenesis" is an improvement over previous strategies as taught by Vajdos, it nonetheless requires extensive planning and analysis and involves the synthesis of 18 sets of degenerate oligonucleotides for the construction of the 4 phage libraries required to comprehensively scan the heterodimeric chains of the antibody (see, in particular, page 416, right column, 2nd paragraph and pages 425-427, Materials and Methods.)

Even after performing this comprehensive scanning mutagenesis of all CDR residues from the particular anti-ErB2 antibody under study, Vajdos would still not have been able to say which CDR residues are actually involved in antigen binding, and which are involved in stabilizing the secondary and tertiary structure of the CDRs within the context of the heavy and light chains as a whole, without the structure of the unbound antigen-binding site of the antibody to aid in their analysis (see, in particular, Discussion, pages 422-425).

Rather, Vajdos needed to perform not only a comprehensive shotgun scanning mutagenesis of all CDR residues of the antibody under study but also needed a structure of the unbound antigen-binding site in hand to gain a sufficient understanding of the contribution of each CDR to antigen-binding that would be required to adequately predict which CDRs can be dispensed with or radically changed. Moreover, given an amino acid substitution that ablated binding, without the crystal structure in hand, still further experimentation would have been required to determine the flexibility in this particular residue, i.e., it's general tolerance or intolerance to change.

That even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function is provided by Rudikoff et al (Proc. Natl. Acad. Sci. USA, 79:1979-1983, March 1982). Rudikoff et al. teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function. Similarly, Colman P. M. (Research in Immunology, 145:33-36, 1994) teaches that even a very conservative substitution may abolish binding or may have very little effect on the binding affinity (see pg. 35, top of left column and pg. 33, right column).

Furthermore, Chien et al. (Proc Natl Acad Sci U S A. 1989 Jul;86(14):5532-6) teaches how changing a single amino acid residue outside and distant from the active site, is also capable of completely eliminating antigen binding (see Chien, page 5536, 3rd paragraph). Chien concludes, "Our results and observations by others of substitutions in JH1 and in JH3 and JH4 suggest that residues distant from the binding site may play an important role in the specificity and affinity of the antigen-binding site." (see Chien, page 5536, 3rd paragraph).

With respect to claims drawn to gene fragments encoding anti-IL-6 antibodies that "bind IL-6 and inhibit the biological activity thereof," the instant specification discloses in the paragraph bridging pages 1-2 that IL-6 has diverse biological activities including induction or inhibition of cellular proliferation, induction of cellular differentiation, however the specification does not define what is meant by an IL-6 biological activity. Thus, for the purposes of examination under 35 U.S.C. § 112, 1st paragraph, the instant claims, given their broadest reasonable interpretation consistent with the instant specification read on gene fragments encoding anti-IL-6 antibodies that bind IL-6 and inhibit any or all IL-6 biological activities.

However, while exemplifying the making of an anti-IL-6 antibody that inhibit the IL-6 dependent proliferation response of IL-6 dependent cell line KT-3, the instant specification does not provide sufficient direction or guidance of the skilled artisan to make gene fragments encoding anti-IL-6 antibodies that inhibit any or all IL-6 biological activities.

Thus, the teachings of the instant specification are extremely narrow relative to the broad scope of the claims at issue.

For example, the skilled artisan recognizes that IL-6 has multiple biological properties that include binding to membrane bound and soluble IL-6R, followed by subsequent interaction with gp130 which induces gp130 signaling, as well as binding to α2-macroglobulin (see, for example, Rose-John et al., J Leukoc Biol. 2006 Aug;80(2):227-36, in particular Introduction on pages 227-228 and Matsuda et al., J Immunol. 1989 Jan 1;142(1):148-52, in particular Discussion on page 151). Each of these distinct IL-6 interactions have distinct consequences on IL-6 biological activity and each interaction is mediated by distinct regions of IL-6. The instant specification does not provide sufficient direction or guidance for the skilled artisan to make and use antibodies that inhibit each of these interactions, thereby inhibiting any or all IL-6 biological activities.

Thus, in view of the teachings of Janeway, Vajdos, Rudikoff, Colman, Chien, Rose-John and Matsuda the instant specification does not provide sufficient teachings or objective evidence to guide the skilled artisan to make and use DNAs encoding the IL-6 antibodies encompassed by the breadth of the instant claims.

Rather, the instant claims encompass an invention of tremendous scope, and essentially calls for trial and error by the skilled artisan using techniques known in the art to begin discovering the claimed invention without assisting the skilled artisan in such an endeavor, which is insufficient to constitute adequate enablement.

The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

Thus, undue experimentation would be required to produce the claimed invention commensurate with the scope of the claims from the written disclosure alone. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

8. Claims 3-11 and 20-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

9. **Applicant is in possession of** a gene fragment coding for a single chain Fv that binds human IL-6 wherein said gene fragment consists of a gene fragment coding for a Vh chain bound to gene fragment coding for a Vl chain, or a gene fragment coding for a single chain Fv that binds human IL-6 wherein said gene fragment consists of a gene fragment coding for a Vh chain bound to gene fragment coding for a Vl chain, wherein CDR1 to CDR3 of Vh are SEQ ID NOs: 5-7 and/or CDR1 to CDR3 of Vl are SEQ ID NOs: 8-10 or a gene fragment coding for a single chain Fv that binds human IL-6 wherein said gene fragment consists of a gene fragment coding for a Vh chain bound to gene fragment coding for a Vl chain, wherein said Vh chain is SEQ ID NO: 2 and said Vl chain is SEQ ID NO: 4, and wherein the above mentioned gene fragments inhibit the IL-6 dependent proliferation response of IL-6 dependent cell line KT-3

However, applicant is not in possession of gene fragments coding for a VH chain or a VL chain of a human anti-human IL-6 antibody, wherein said gene fragments comprise, for example, anything from a single CDR from a Vh or Vl to a full length Vh or Vl, or gene fragments coding for a single chain Fv human anti-human IL-6 antibody consisting of defined Vh and Vl genes wherein the gene fragments comprise amino acid deletions and/or substitutions and/or additions in the Vh and/or Vl chains, without an upper limit on the number of changes, and wherein the above mentioned gene fragments inhibit any or all IL-6 biological activities.

rather than what it is").

Moreover, according to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, especially page 1106 3rd column, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

What constitutes a "representative number" is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. See, MPEP 2163 II.A.3a.ii.

Applicant is directed to the Revised Guidelines for the Examination of Patent Applications Under the 35 U.S.C.112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No.4, pages 1099-1111, Friday January 5, 2001).

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 3, 7 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Garrone et al. (United States Patent No. 5,959,085).

Garrone teaches nucleotides coding for anti-human IL-6 antibodies including scFv antibodies wherein said antibodies may be used prophylactically to prevent or inhibit the occurrence of symptoms associated with the antigen of interest, such as IL-6 (see, in particular, column 2, 3rd paragraph to column 5, 1st paragraph; column 9, 6th paragraph; column 12, 1st paragraph; and column 29, 1st paragraph to column 30, 1st paragraph).

Thus, the instant claims are anticipated by Garrone.

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary Skelding whose telephone number is 571-272-9033. The examiner can normally be reached on Monday - Friday 8:00 a.m. - 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Zachary Skelding, Ph.D.
Patent Examiner
October 4, 2007

MICHAIL BELYAVSKYI, PH.D.
PATENT EXAMINER

10/4/07

The instant specification does not provide adequate written description of the broad genus of gene fragments encompassed by instant claims because relevant identifying characteristics for the gene fragments encompassed by the instant claims, such as the particular ***structural or other physical and/or chemical characteristics that are critical to the function*** of the claimed gene fragments, i.e., inhibiting the biological activity of IL-6, are not disclosed.

Since the amino acid sequence of a protein determines its structural and functional properties the changes that can be tolerated in a antibody while retaining similar biological activity or structural specificity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function.

The instant specification does not provide sufficient direction or guidance as to which particular amino acid residues of the claimed antibody can be changed and the specific nature of the change, i.e., deletion, insertion or substitution, without ablating the ability of the antibody to bind IL-6, essentially for the reasons stated in Section 7 above with respect to the unpredictability in the art with respect to the structural flexibility and functional importance vis a vis antibody binding of any given CDR and or framework residue within an antibody. Moreover, the instant specification does not provide sufficient direction or guidance as to the common structure of IL-6 that is responsible for its various biological activities and thus the instant specification does not demonstrate possession of antibodies that bind iL-6 and inhibit and or all IL-t6 biological activities, essentially for the reasons stated in Section 7 above with respect to the diverse and distinct IL-6 interactions with IL-6R, gp130 and α2-macroglobulin.

Without this guidance or direction the skilled artisan would not consider applicant to be in possession of the claimed genus of gene fragments because the skilled artisan recognizes that even seemingly minor changes made without guidance or direction as to the relationship between the particular amino acid sequence of the instantly claimed gene fragments and its ability to bind antigen, can dramatically affect antigen-antibody binding.

Sufficient description to show possession of such a genus "may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1567, 43 USPQ2d 1398, 1405 (Fed. Cir. 1997). Possession may not be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features. *See University of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 69 USPQ2d 1886 (Fed. Cir. 2004).

Without a correlation between structure and function, the claim does little more than define the claimed invention by function. That is not sufficient to satisfy the written description requirement. *See Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406 ("definition by function ... does not suffice to define the genus because it is only an indication of what the gene does,